Supplementary Online Content

Issels RD, Lindner LH, Verweij J, et al. Effect of neoadjuvant chemotherapy plus regional hyperthermia on long-term outcomes among patients with localized high-risk soft tissue sarcoma: the EORTC 62961-ESHO 95 randomized clinical trial. *JAMA Oncol*. Published online February 15, 2018. doi:10.1001/jamaoncol.2017.4996

This supplementary material has been provided by the authors to give readers additional information about their work.

Online Supplementary Materials

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eText 1. Reasons patients were excluded from the study.

Seven patients of the NACT-RHT group (6 withdrew of consent, 1 metastatic disease), and 5 patients of the NACT-alone group (4 withdrew of consent, 1 metastatic disease) were excluded. Those patients never started their allocated treatment after randomization. The withdrawal of consent of the 4 patients in the NACT-alone group occurred because the patients randomly allocated to receive no hyperthermia did not accept being treated without hyperthermia. The withdrawal of consent of the 6 patients in the NACT-RHT group occurred because of logistic reasons, or because of their final refusal of the first hyperthermia application. In the other two patients of each treatment arm, evidence of metastatic disease was documented before start of the allocated treatment which was not performed because of the exclusion criteria.

eTable 1: Summary of efficacy measures in the Intention-to-Treat population.

	NACT-RHT (N=162)	NACT-alone (N=167)	P-Value
Median follow-up time (years [IQR])			
Median (IQR)	10.9 (10.3-12.3)	12.6 (10.8-13.7)	0.218*
Local progression-free survival			
Median duration – years (95% CI)	5.6 (2.9–8.7)	2.4 (1.7–4.2)	0.002*
Hazard ratio (95% CI)	0.65 (0.49–0.86)		
Disease-free survival			
Median duration – years (95% CI)	2.8 (2.0–4.9)	1.5 (1.1–2.1)	0.013*
Hazard ratio (95% CI)	0.71 (0.55–0.93)		
Survival			
Median duration – years (95% CI)	15.4 (6.6 to >17.0)	6.2 (3.2–10.3)	0.037*
Hazard ratio (95% CI)	0.73 (0.54–0.98)		
Response to induction therapy			0.002+
No measurable disease – no. (%)	48 (29.6)	43 (25.7)	
Measurable disease – no. (%)	114 (70.4)	124 (74.3)	
Complete response – no. (%)	3 (2.6)	1 (0.8)	
Partial response – no. (%)	31 (27.2)	15 (12.1)	
Stable disease – no. (%)	63 (55.3)	73 (58.9)	
Progressive disease – no. (%)	8 (7.0)	25 (20.2)	
Not evaluable – no. (%)	9 (7.9)	10 (8.1)	
Overall response (%)	34 (29.8)	16 (12.9)	

*log-rank test, + chi-square test CR+PR vs. SD+PD

eTable 2: Distribution of radiotherapy between R0 and R1 resected patients.

	NACT plus RHT		NACT alone		Odds ratio
Surgery	Received RT (N=58)	Did not receive RT (N=26)	Received RT (N=61)	Did not receive RT (N=16)	
R0 (N=92)	32	19	31	10	1.84 (CI 95%: 0.74-4.58)
R1 (N=69)	26	7	30	6	1.36 (CI 95%: 0.40-4.52)

eTable 3: Effect of radiotherapy in different treatment groups (R0, R1, R0+R1) on local progression-free survival.

			Local Progression-free Survival Univariate	
Factor	**Radio-therapy**	**No.**	**HR (95% CI)**	**P Value**
R0		92		
NACT-RHT	no	19		
	yes	32	0.75 (0.35-1.61)	0.466
NACT-alone	no	10		
	yes	31	1.04 (0.41-2.61)	0.940
R1		69		
NACT-RHT	no	7		
	yes	26	0.35 (0.13-0.93)	0.035
NACT-alone	no	6		
	yes	30	0.39 (0.15-1.00)	0.050
R0+R1		161		
NACT-RHT	no	26		
	yes	58	0.65 (0.36-1.17)	0.151
NACT-alone	no	16		
	yes	61	0.72 (0.38-1.38)	0.319